THU0507 LONG-TERM EXPERIENCE WITH ADALIMUMAB FOR THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS. 5- YEAR DATA FROM THE GERMAN BIKER REGISTRY

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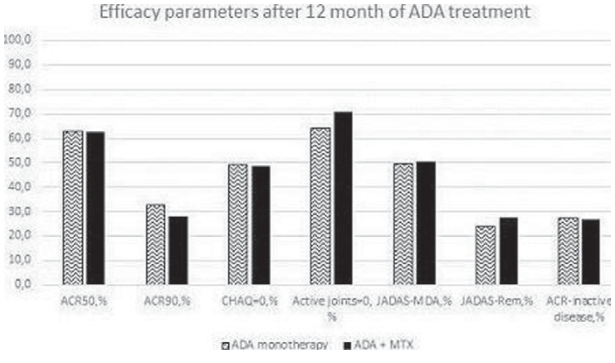
Background: Since the approval of Adalimumab (ADA) for treatment of juvenile idiopathic arthritis (JIA), it has become a valuable option, which significantly improved the outcome of patients.
Objectives: To report efficacy (as observed) and safety of ADA in clinical practice.
Methods: Data from the German BiKeR register from 2011 to 2016 are reported. Baseline patient characteristics, treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS score and improvement of functional status (Childhood Health Assessment Questionnaire disability index, CHAQ), JIA-ACR-scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.
Results: 589 non-systemic JIA patients exposed to Adalimumab with at least one follow-up report were identified in the German BIKER registry, representing 1143.9 patient years (PY) of exposure to ADA and 1206.5 observation years including 90 days after discontinuation. At Baseline, 58.2% received combination with methotrexate (MTX). Patients on combination treatment had more frequently ANA, less frequently HLA-B27, had higher JADAS 10 and more often received systemic steroids (9.9% vs. 22.2%, p=0.0002). ADA dosage was 0.8mg/kg in both cohorts.
At month 12 JIA-ACR 30/50/70/90 and JADAS-MDA/-remission/ACR-inactive disease was reached by 66/63/49/33/50/24/27% on monotherapy with ADA and 68/63/45/28%/50/28/27 on combination of ADA and MTX (not significant). Response rates at month 24 were 67/66/54/35/65/32/29% on ADA monotherapy and 67/61/46/31/57/35/30% on ADA+MTX combination cohort (not significant).
The rate (/100PY) of all adverse events (AE)/serious AE/infections/serious infections/uveitis events was 52.3/2.2/16.4/4.6 upon monotherapy and 65.3/5.1/2.3/16.4/6.2 upon combination. Only rates for any AE were significantly higher upon combination (p=0.008) as well as rate of elevated transaminase (p=0.01). Rate of patients with an uveitis event was higher upon combination (9.6% vs. 5.3%, p=0.007)

Table 1

	ADA monotherapy	ADA + MTX	P
N, female (%)	223 (70)	343 (70)	n.s.
Age onset/disease duration; mean (SD)	7.1 (±4.3)/6.0 (3.7)	6.5 (4.5)/5.0 (3.7)	n.s.
RF neg. Poylarthritis, n (%)	77 (34.5)	126 (36.7)	n.s.
RF pos. Poylarthritis, n (%)	7 (3.1)	17 (5.0)	n.s.
pers. Oligoarthritis, n (%)	12 (5.4)	29 (8.5)	n.s.
ext. Oligoarthritis, n (%)	59 (26.5)	95 (27.7)	n.s.
ERA, n (%)	49 (22.0)	47 (13.7)	p=0.01
PsA, n (%)	15 (6.7)	22 (6.4)	n.s.
unclassified JIA, n (%)	4 (1.8)	7 (2.0)	n.s.
ANA/B27, n (%)	111 (49.8)/ 56 (25.1)	210 (61.2)/ 57 (16.6)	p=0.009/ p=0.02
Comorbidity Uveitis, n (%)	19 (8.5)	32 ((9.3)	n.s.
Baseline active joints mean (SD)	3.5 (5.6)	3.8 (5.5)	n.s.
Phy VAS mean (SD)	37.6 (28.6)	42.7 (28.3)	n.s.
Pat VAS mean (SD)	27.9 (24.9)	30.9 (24.9)	n.s.
CHAQ mean (SD)	0.4 (0.6)	0.4 (0.6)	n.s.
ESR mean (SD)	14.3 (15.2)	18.1 (17.7)	n.s.
CRP mean (SD)	4.3 (7.4)	8.3 (15.8)	n.s.
Baseline JADAS10 mean (SD)	9.9 (7.0)	11.3 (7.1)	p=0.02



Conclusions: Adalimumab demonstrated high response rates and an acceptable risk profile. Efficacy and safety of monotherapy was not inferior to combination therapy with MTX.
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THU0508 PSYCHOLOGICAL FEATURES OF CHILDREN WITH RHEUMATIC DISEASES

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Background: Rheumatic diseases (RD) in children are characterized by a wide spectrum of clinical manifestations, and variability of flow, the defeat of many body systems, including the musculoskeletal system, which often leads to early disability. The disease brings the children not only physical suffering and psychological distress as a result of the pathological process may be sufficiently stable defects in appearance, affecting the minds of the growing person.
Objectives: To study the psychological characteristics of children with rheumatic diseases.
Methods: 167 patients with RD were examined in the period from 2008 to 2015. In the I group included 115 children with juvenile idiopathic arthritis (JIA) (mean age 11,9±3,4 years), II group consisted of 34 children with juvenile scleroderma (JS) (mean age 12,4±2,8 years), III - 18 children with systemic lupus erythematosus (SLE) (mean age 13,1±1,7 years). As control group examined 30 healthy children aged 9–17 years (mean age 12,93±0,4 years). To investigate the expression of reactive anxiety (RA) and personal anxiety (PA) in children older than 9 years was used scale Ch.D.Spielberg. In order to study the intensity of anxiety was used M.Luscher color test. To identify the individual psychological characteristics of the individual patient questionnaire used G.J.Eysenck for teenagers, consisting of 60 questions, including the scale of extroversion, introversion, neuroticism and the scale of "the scale of lies". Testing patients and interpretation of the results was carried out together with a psychologist.
Results: The test Spielberg results indicate that significantly more ($P<0.001$), medium and high levels of anxiety both reactive and personal, occurred in children with RD. This suggests the presence of children with RD border states with the threat of self-assessment features, reducing the threshold of resistance to stressful situations. The average RA and PA indices were significantly higher ($P<0.001$) in children with RD in comparison with indicators of reactive and personal anxiety in children in the control group (46,09±0,88 points for the JS, 43,77±1,37 points for JIA, 45,07±1,83 points for SLE and 27,6±0,62 points for the control group, respectively, RA; 42,22±1,68 points for the JS, 37,84±1,27 points for the JIA, 44,76±0,88 points for SLE and 28,7±0,51 points, respectively, RA for the control group).
Results of the study with the help of M.Lusher's color test revealed the intensity of anxiety in children with JS, SLE and JIA. Evaluation results of the study showed that children and adolescents with RD clearly manifested trend bias pri-mary colors on the 6,7,8 positions, and more - in the first place.
In order to identify characteristics of temperament in patients aged 13–17 years were asked to complete a questionnaire G.J.Eysenck for undergrowth Cove. The majority of surveyed teens both clinical groups manifest emotional instability (73.3% of patients with JS and 70% of patients with JIA) and features typical of introversion (60% of patients with SS and 68% of patients with JIA) (verified differences were found) between the groups. According to G.J.Eysenck, high rates of introversion in conjunction with emotional instability correspond to the alarm state.
Conclusions: As a result, psychometric studies found that the characteristic of emotional tension, anxiety, isolation for children with RD.
Disclosure of Interest: None declared
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THU0509 IMPROVEMENT OF DISEASE ACTIVITY IN PATIENTS WITH COLCHICINE-RESISTANT FMF, HIDS/MKD AND TRAPS ASSESSED BY AUTOINFLAMMATORY DISEASE ACTIVITY INDEX (AIDAI): RESULTS FROM THE CLUSTER TRIAL

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Background: AIDAI is a novel validated tool for assessment of disease activity in autoinflammatory diseases.[1] CLUSTER study (NCT02059291) demonstrated that canakinumab (CAN; an anti- IL-1β antibody) is efficacious in resolving active flare and in preventing new flare in patients (pts) with colchicine resistant familial Mediterranean fever (crFMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS).[2]

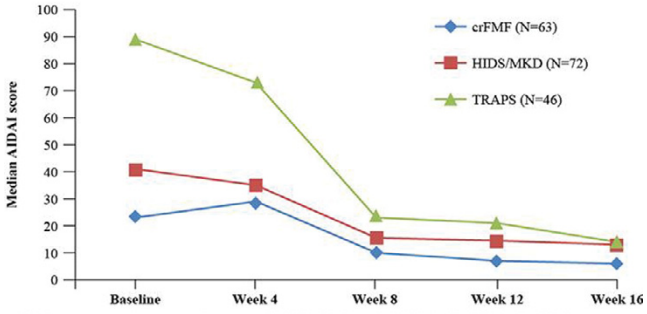
Objectives: To assess AIDAI score and evaluate correlation between AIDAI and disease/response characteristics over 16 weeks (wks) of CAN treatment in CLUSTER.
Methods: CLUSTER study design and results have been presented.[2] AIDAI was calculated as the sum of 12 items[1] for 30 consecutive days. AIDAI score was calculated if the first score was recorded ≥29 days before baseline (BL). Missing items were imputed beyond last evaluable measurement by LOCF. Proportion of pts with inactive disease (ID; AIDAI score <9) was calculated at Wk 16. Correlation analysis of AIDAI with C-reactive protein (CRP), serum amyloid A (SAA), physician global assessment (PGA) and sheehan disability score (SDS), and child health questionnaire–psychological/physical (CHQ–PsCS/PCS) and short form 12–physical/mental (SF12–PCS/MCS) component summaries were performed at BL and Wk 16, with significance set at $p<0.05$.
Results: Median AIDAI scores decreased over time (Fig 1). Proportion of pts with ID at Wk 16 was 52% in crFMF, 40% in HIDS/MKD and 46% in TRAPS cohorts. AIDAI at Wk 16 correlated significantly with: SDS in all 3 cohorts; PGA in HIDS/MKD and TRAPS; SF12–MCS in crFMF and HIDS/MKD (Table 1). CRP and SAA did not correlate with AIDAI.

Table 1. Correlation between AIDAI and disease activity/response variables at Week 16

	Correlation coefficient (95% CI)		
	crFMF (N=63)	HIDS/MKD (N=72)	TRAPS (N=46)
CRP	–0.12 (–0.36; 0.14)	0.23 (–0.01; 0.45)	0.12 (–0.19; 0.42)
SAA	–0.01 (–0.27; 0.25)	–0.05 (–0.30; 0.21)	0.06 (–0.26; 0.37)
PGA	0.23 (–0.02; 0.46)	**0.35§ (0.12; 0.55)**	**0.73* (–0.54; 0.85)**
CHQ – PsCS	–0.18 (–0.56; 0.26)	–0.25 (–0.55; 0.11)	–0.33 (–0.72; 0.22)
CHQ – PCS	–0.33 (–0.66; 0.11)	**–0.46§ (–0.70; –0.14)**	–0.48 (–0.80; 0.04)
SF12 – PCS	–0.26 (–0.57; 0.11)	–0.23 (–0.68; 0.35)	**–0.52‡ (–0.81; –0.03)**
SF12 – MCS	**–0.45‡ (–0.70; –0.10)**	**–0.55‡ (–0.84; –0.03)**	0.09 (–0.43; 0.56)
SDS	**0.47† (0.22; 0.67)**	**0.37§ (0.10; 0.59)**	**0.41‡ (0.06; 0.67)**

*$p<0.0001$; †$p<0.001$; §$p<0.01$; ‡$p<0.05$.

Fig 1. Median AIDAI scores over 16 weeks



AIDAI score was calculated as the sum of all 12 daily items (YES=1 or NO=0) during 30 days.
Missing AIDAI assessments between first and last AIDAI assessments were imputed as NO.
Missing AIDAI assessments after last AIDAI assessment were imputed as NO.
LOCF, last observation carried forward.

Conclusions: CAN demonstrated rapid and sustained disease control assessed with AIDAI over 16 wks. Approximately half of crFMF and TRAPS pts, and 40% of HIDS/MKD patients had inactive disease after 16 wks of treatment. AIDAI improvements at Wk 16 correlated with patient and physician driven evaluations (PGA, SF12–MCS and SDS). CRP and SAA are indicators of response to treatment, rather than a disease activity parameter.
References:
[1] Piram M, et al. Ann Rheum Dis. 2014;73: 2168–73.
[2] De Benedetti F, et al. Ann Rheum Dis. 2016;75:615–6.
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THU0510 UKRAINIAN REGISTRY OF JIA PATIENTS RECEIVING BIOLOGICS: IMPLEMENTATION INTO CLINICAL PRACTICE AND RECENT DATA

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Background: The situation with a treatment of juvenile idiopathic arthritis (JIA) is complicated in Ukraine. Mainly due to financial reason biological therapy is hardly accessible for Ukrainian patients. Nevertheless, some patients with JIA receive biologics within governmental programme. Clinical data of these patients were scattered and not systematized until 2014. The Task Force of Ukrainian Association of rheumatologists, by analogy to other European registries, has developed a registry of JIA patients receiving biologics. Ukrainian register of JIA patients is an observational, prospective, non-interventional clinical study.
Objectives: The main aim of Ukrainian register of JIA patients is an assessment of long-term safety, efficacy and cost of biological treatment of JIA. in the routine clinical practice.
Methods: 33 clinical sites from different regions of Ukraine are participating. Inclusion criteria: i) diagnosis of JIA: ii)age ≤2 years old, iii)planned start of biological therapy due to JIA; iv)negative screening for tuberculosis; v)provided informed consent. Patients have undergone standard clinical assessment every 3 months. Disease activity is measured using JADAS27 in all age groups. ANA, HLAB27, RF and anti-CCP detection are highly recommended. Uveitis and other comorbid conditions should also be fixed.
Results: 339 patients were enrolled into the study during 3 years. 64% of patients are girls. Mean age–10.98±4.41 years, with mean disease duration –5.81±3.48 years. The duration of the period between diagnosis and biologics start was 54.31±40.28 months. Comorbid conditions were found in 41.03% patients. In 14.65% of the patients uveitis was diagnosed. Most common JIA subtypes in patients receiving biologics are pJIA with negative RF (45%), sJIA (20%), enthesitis-associated JIA (11%) and persistent oligoarthritis (11%). 67.3% of enrolled patients received adalimumab (ADA); 27.9%>tocilizumab (TOZ) and 4.8%>etanercept, respectively. During observational period biologics was discontinued in 19.8% of patients due to different reasons: adverse events were observed in 6.7% (ADA) and 16.7% (TOZ), insufficient efficiency of 23.3% (ADA) and 33.3% (TOZ), remission - 6.7% (ADA); drug absence - 63.3% (ADA) and 50% (TOZ), respectively. Comparative analysis of ADA and TOZ efficacy was performed in the 144 patients with pJIA with negative RF. Administration either ADA or TOZ resulted in statistically significant reducing of disease activity according to JADAS27. In ADA group after 3 months of administration JADAS27 decreased from 16.3±10.3 to 10.0±7.8 ($p<0.00001$). In TOZ group after 3 months of administration JADAS27 reduced from 22.2±12.2 to 13.1±9.1 ($p=0.0012$). The functional disability of the patients also statistically significant decrease in both treatment group starting from 3 months of administration: 1.1±0.8 to 0.7±0.7 ($p=0.0081$) in ADA and 1.6±1.0 to 1.0±0.7 in TOZ, respectively.
Conclusions: Ukrainian national registry of JIA patients provides real-life long-term data concerning safety, efficacy, outcomes and comparative analysis of biologics in Ukrainian population of JIA patients. Data collection continues and the data received expected to be a background for clinical decision-making in future.
Disclosure of Interest: None declared
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THU0511 TOCILIZUMAB IS A PROMISING TREATMENT OPTION FOR THERAPY RESISTENT JUVENILE LOCALISED SCLERODERMA PATIENTS

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Background: Juvenile localised scleroderma (jlSc) is an orphan disease. Most patient respond to treatment ot methotrexate or mycophenolate. In case of nonresponse or partial response, based on the promising tocilizumab (TOC) data of adult systemic sclerosis studies, TOC seems to be a promising option. There is no publication regarding the effectiveness of tocilizumab in jLS.
Objectives: To assess the effectivity of TOC in jlSC patients, who had nonresponse or partial response on conventional therapy.
Methods: Participants of the pediatric rheumatology email board were asked, if they follow patients with jlSc, who are treated with TOC. Clinical characteristics and the response to TOC was assessed.
Results: Six centers responded to the survey from the email board, with around 800 participatns, and reported 11 patients. The mean age of the patients at disease onset was 5.5 years. Disease duration at time of the intiation of TOC was 53.5. months (range 9 to 109). 5 patients had linear subtype, 3 of them with facial involvement, 2 of them Parry Romberg and one of them coup de sabre. Three had generalized subtype, 2 mixed subtype and 1 limited subtype/morphea. Before starting TOC patients received 10/11 Methotrexate, 7/11 Mycophenolate, 1 abatacept and 1 anti-TNF therapy. Reason to start TOC was in 9 patients increase in Localised Scleroderma Activity Index [1] (mLoSSI). In two patients increased extracutaneous activity was the indication, in one increased activity of arthritis and in the other increased activity of the central nervous system involvement.